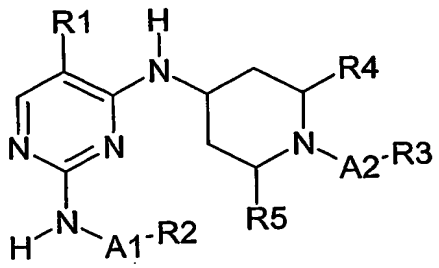
Patent Claims

1. A compound of formula 1,



(1)

in which

R1 is a mono- or bicyclic aromatic radical substituted by R11, R12, R13 and R14, wherein R1 is selected from the group consisting of phenyl, naphthyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, indolyl, benzimidazolyl, furanyl (furyl), benzofuranyl (benzofuryl), thiophenyl (thienyl), benzothiophenyl (benzothienyl), thiazolyl, isoxazolyl, pyridinyl, pyrimidinyl, quinolinyl and isoquinolinyl, where

R11 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, aryl, aryl-1-4C-alkyl, aryloxy, aryl-1-4C-alkoxy, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl, or together with R12 methylenedioxy or ethylenedioxy,

R12 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl or hydroxyl, or together with R11 methylenedioxy or ethylenedioxy,

R13 is hydrogen, 1-4C-alkyl or halogen and

R14 is hydrogen, 1-4C-alkyl or halogen,

where

aryl is phenyl or substituted phenyl having one, two or three substituents selected from the group consisting of 1-4C-alkyl, 1-4C-alkoxy, carboxyl, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl, nitro, trifluoromethoxy, hydroxyl, cyano and mixtures thereof,

R2 is a mono- or bicyclic aromatic radical substituted by R21, R22, R23 and R24, wherein R2 is selected from the group consisting of phenyl, naphthyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, indolyl, benzimidazolyl, furanyl (furyl), benzofuranyl (benzofuryl), thiophenyl (thienyl), benzothiophenyl (benzothienyl), thiazolyl, isoxazolyl, pyridinyl, pyrimidinyl, quinolinyl and isoquinolinyl, where

R21 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, aryl, aryl-1-4C-alkyl, aryloxy, aryl-1-4C-alkoxy, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-

alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl, or together with R22 methylenedioxy or ethylenedioxy,

R22 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl or hydroxyl, or together with R21 methylenedioxy or ethylenedioxy,

R23 is hydrogen, 1-4C-alkyl or halogen and

R24 is hydrogen, 1-4C-alkyl or halogen,

where

aryl is phenyl or substituted phenyl having one, two or three substituents selected from the group consisting of 1-4C-alkyl, 1-4C-alkoxy, carboxyl, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl, nitro, trifluoromethoxy, hydroxyl, cyano and mixtures thereof,

R3 is a mono- or bicyclic aromatic radical substituted by R31, R32, R33 and R34, wherein R3 is selected from the group consisting of phenyl, naphthyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, indolyl, benzimidazolyl, furanyl (furyl), benzofuranyl (benzofuryl), thiophenyl (thienyl), benzothiophenyl (benzothienyl), thiazolyl, isoxazolyl, pyridinyl, pyrimidinyl, quinolinyl and isoquinolinyl,

where

R31 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, aryl, aryl-1-4C-alkyl, aryloxy, aryl-1-4C-alkoxy, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl, or together with R32 methylenedioxy or ethylenedioxy,

R32 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl or hydroxyl, or together with R31 methylenedioxy or ethylenedioxy,

R33 is hydrogen, 1-4C-alkyl or halogen and

R34 is hydrogen, 1-4C-alkyl or halogen,

where

aryl is phenyl or substituted phenyl having one, two or three substituents selected from the group consisting of 1-4C-alkyl, 1-4C-alkoxy, carboxyl, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl, nitro, trifluoromethoxy, hydroxyl, cyano and mixtures thereof,

R4 is hydrogen or methyl,

R5 is hydrogen or methyl,

A1 is 1-3C-alkylene or ethyleneoxy ($-CH_2-CH_2-O-$) and

A2 is 1-3C-alkylene or ethyleneoxy ($-CH_2-CH_2-O-$),

or a salt thereof.

2. A compound of formula 1 according to claim 1,

in which

R1 is a mono- or bicyclic aromatic radical substituted by R11, R12, R13 and R14, wherein R1 is selected from the group consisting of phenyl, naphthyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, indolyl, benzimidazolyl, furanyl (furyl), benzofuranyl (benzofuryl), thiophenyl (thienyl), benzothiophenyl (benzothienyl), thiazolyl, isoxazolyl, pyridinyl, pyrimidinyl, quinolinyl and isoquinolinyl,

where

R11 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, aryl, aryl-1-4C-alkyl, aryloxy, aryl-1-4C-alkoxy, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl,

R12 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl or hydroxyl,

R13 is hydrogen, 1-4C-alkyl or halogen and

R14 is hydrogen, 1-4C-alkyl or halogen,

where

aryl is phenyl or substituted phenyl having one, two or three substituents selected from the group consisting of 1-4C-alkyl, 1-4C-alkoxy, carboxyl, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl, nitro, trifluoromethoxy, hydroxyl, cyano and mixtures thereof,

R2 is a mono- or bicyclic aromatic radical substituted by R21, R22, R23 and R24, wherein R2 is selected from the group consisting of phenyl, naphthyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, indolyl, benzimidazolyl, furanyl (furyl), benzofuranyl (benzofuryl), thiophenyl (thienyl), benzothiophenyl (benzothienyl), thiazolyl, isoxazolyl, pyridinyl, pyrimidinyl, quinolinyl and isoquinolinyl,

where

R21 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, aryl, aryl-1-4C-alkyl, aryloxy, aryl-1-4C-alkoxy, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl,

R22 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl or hydroxyl,

R23 is hydrogen, 1-4C-alkyl or halogen and

R24 is hydrogen, 1-4C-alkyl or halogen,

where

aryl is phenyl or substituted phenyl having one, two or three substituents selected from the group consisting of 1-4C-alkyl, 1-4C-alkoxy, carboxyl, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl, nitro, trifluoromethoxy, hydroxyl, cyano and mixtures thereof,

R3 is a mono- or bicyclic aromatic radical substituted by R31, R32, R33 and R34, wherein R3 is selected from the group consisting of phenyl, naphthyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, indolyl, benzimidazolyl, furanyl (furyl), benzofuranyl (benzofuryl), thiophenyl (thienyl), benzothiophenyl (benzothienyl), thiazolyl, isoxazolyl, pyridinyl, pyrimidinyl, quinolinyl and isoquinolinyl,

where

R31 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl,

carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, aryl, aryl-1-4C-alkyl, aryloxy, aryl-1-4C-alkoxy, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl,

R32 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl or hydroxyl,

R33 is hydrogen, 1-4C-alkyl or halogen and

R34 is hydrogen, 1-4C-alkyl or halogen,

where

aryl is phenyl or substituted phenyl having one, two or three substituents selected from the group consisting of 1-4C-alkyl, 1-4C-alkoxy, carboxyl, 1-4C-alkoxycarbonyl, halogen, trifluoromethyl, nitro, trifluoromethoxy, hydroxyl, cyano and mixtures thereof,

R4 is hydrogen,

R5 is hydrogen,

A1 denotes 1-3C-alkylene and

A2 denotes 1-3C-alkylene,

or a salt thereof.

3. A compound of formula 1 according to claim 1,

in which

R1 is an aromatic radical substituted by R11, R12, R13 and R14, wherein R1 is selected from the group consisting of phenyl, furanyl (furyl) and thiophenyl (thienyl),

where

R11 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl, or together with R12 methylenedioxy or ethylenedioxy,

R12 is hydrogen or halogen, or together with R11 methylenedioxy or ethylenedioxy,

R13 is hydrogen and

R14 is hydrogen,

R2 is an aromatic radical substituted by R21, R22, R23 and R24, wherein R2 is selected from the group consisting of pyridinyl and pyrimidinyl,

where

R21 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy or halogen,

R22 is hydrogen or halogen,

R23 is hydrogen and

R24 is hydrogen,

R3 is an aromatic radical substituted by R31, R32, R33 and R34, wherein R3 is selected from the group consisting of phenyl and pyridinyl,

where

R31 is hydrogen, 1-4C-alkyl, hydroxy-1-4C-alkyl, 1-4C-alkoxy, 2-4C-alkenyloxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkoxycarbonyl, carboxy-1-4C-alkyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, halogen, hydroxyl, trifluoromethyl, nitro, amino, mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, 1-4C-alkoxycarbonylamino, 1-4C-alkoxy-1-4C-alkoxycarbonylamino or sulfonyl,

R32 is hydrogen or halogen,

R33 is hydrogen and

R34 is hydrogen,

R4 is hydrogen or methyl,

R5 is hydrogen or methyl,

A1 is 1-3C-alkylene or ethyleneoxy (-CH_2-CH_2-O-) and

A2 is 1-3C-alkylene or ethyleneoxy (-CH_2-CH_2-O-),

or a salt thereof.

4. A compound of formula 1 according to claim 1,

in which

R1 is an aromatic radical substituted by R11, R12, R13 and R14, wherein R1 is selected from the group consisting of phenyl, furanyl (furyl) and thiophenyl (thienyl),

where

R11 is hydrogen, 1-4C-alkoxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, halogen, hydroxyl or mono- or di-1-4C-alkylamino, or together with R12 methylenedioxy or ethylenedioxy,

R12 is hydrogen or halogen, or together with R11 methylenedioxy or ethylenedioxy,

R13 is hydrogen and

R14 is hydrogen,

R2 is an aromatic radical substituted by R21, R22, R23 and R24, wherein R2 is selected from the group consisting of pyridinyl and pyrimidinyl,

where

R21 is hydrogen,

R22 is hydrogen,

R23 is hydrogen and

R24 is hydrogen,

R3 is an aromatic radical substituted by R31, R32, R33 and R34, wherein R3 is selected from the group consisting of phenyl and pyridinyl,

where

R31 is hydrogen, 1-4C-alkoxy or halogen,

R32 is hydrogen,

R33 is hydrogen and

R34 is hydrogen,

R4 is hydrogen or methyl,

R5 is hydrogen or methyl,

A1 denotes methylene, ethylene, ethylidene [-CH(CH_3)-] or ethyleneoxy (-CH_2-CH_2-O-) and

A2 denotes methylene, ethylene, ethylidene [-CH(CH_3)-] or ethyleneoxy (-CH_2-CH_2-O-),

or a salt thereof.

5. A compound of formula 1 according to claim 1,

in which

R1 is an aromatic radical substituted by R11, R12, R13 and R14, wherein R1 is selected from the group consisting of phenyl, furanyl (furyl) and thiophenyl (thienyl),

where

R11 is hydrogen, 1-4C-alkoxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, halogen, hydroxyl or mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, or together with R12 methylenedioxy or ethylenedioxy,

R12 is hydrogen or halogen, or together with R11 methylenedioxy or ethylenedioxy,

R13 is hydrogen and

R14 is hydrogen,

R2 is an aromatic radical substituted by R21, R22, R23 and R24, wherein R2 is selected from the group consisting of pyridinyl and pyrimidinyl,

where

R21 is hydrogen,

R22 is hydrogen,

R23 is hydrogen and

R24 is hydrogen,

R3 is an aromatic radical substituted by R31, R32, R33 and R34, wherein R3 is selected from the group consisting of phenyl and pyridinyl,

where

R31 is hydrogen, 1-4C-alkoxy or halogen,

R32 is hydrogen,

R33 is hydrogen and

R34 is hydrogen,

R4 is hydrogen or methyl,

R5 is hydrogen or methyl,

A1 denotes methylene, ethylene, ethylidene [-CH(CH_3)-] or ethyleneoxy (-CH_2-CH_2-O-) and

A2 denotes methylene, ethylene, ethylidene [-CH(CH_3)-] or ethyleneoxy (-CH_2-CH_2-O-),

or a salt thereof.

6. A compound of formula 1 according to claim 1,

in which

R1 is furanyl (furyl), thiophenyl (thienyl) or phenyl substituted by R11 and R12,

where

R11 is hydrogen, 1-4C-alkoxy, 1-4C-alkylcarbonyl, carboxyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, halogen, hydroxyl or mono- or di-1-4C-alkylamino, 1-4C-alkylcarbonylamino, or together with R12 methylenedioxy or ethylenedioxy,

R12 is hydrogen or halogen, or together with R11 methylenedioxy or ethylenedioxy,

R2 is pyridinyl,

R3 is phenyl,

R4 is hydrogen,

R5 is hydrogen,

A1 denotes methylene and

A2 denotes methylene,

or a salt thereof.

7. A compound of formula 1 according to claim 1,

in which

R1 is furanyl (furyl), thiophenyl (thienyl) or phenyl substituted by R11 and R12,

where

R11 is hydrogen, 1-4C-alkoxy, carboxyl, aminocarbonyl, halogen or di-1-4C-alkylamino and

R12 is hydrogen,

R2 is pyridinyl,

R3 is phenyl,

R4 is hydrogen,

R5 is hydrogen,

A1 denotes methylene and

A2 denotes methylene,

or a salt thereof.

8. A compound of formula 1 according to claim 1, wherein R2 is 2-pyridinyl or 4-pyridinyl.

9. A compound of formula 1 according to claim 1, wherein R3 is phenyl.

10. A compound of formula 1 according to claim 1, wherein R1 is furanyl (furyl), thiophenyl (thienyl) or phenyl substituted by R11 and R12, where R11 is hydrogen, 1-4C-alkoxy, carboxyl, aminocarbonyl, halogen or di-1-4C-alkylamino and R12 is hydrogen.

11. A compound of formula 1 according to claim 1, wherein R1 is furanyl (furyl), thiophenyl (thienyl) or phenyl substituted by R11 and R12, where R11 is hydrogen, 1-4C-alkoxy, halogen, di-1-4C-alkylamino, aminocarbonyl, carboxyl, 1-4C-alkylcarbonylamino, hydroxyl, 1-4C-alkylcarbonyl or together with R12 methylenedioxy or ethylenedioxy and R12 is hydrogen, halogen or together with R11 methylenedioxy or ethylenedioxy.

12. A compound of formula 1 according to claim 1, wherein R1 is 2-furanyl or 3-furanyl.

13. A compound of formula 1 according to claim 1, wherein R1 is 2-thiophenyl or 3-thiophenyl.

14. A compound of formula 1 according to claim 1, wherein R1 is selected from the group of phenyl, 4-methoxyphenyl, 4-chlorophenyl, 4-dimethylaminophenyl, 4-aminocarbonylphenyl, 4-carboxyphenyl, 3-chloro-4-fluorophenyl, 3-acetylaminophenyl, benzo[1,3]dioxol-5-yl, 3-hydroxyphenyl, 4-hydroxyphenyl, 4-acetylphenyl, 3-acetylphenyl, 4-acetylaminophenyl, 4-dimethylaminocarbonyl-phenyl and 4-aminocarbonylphenyl.

15. A compound of formula 1 according to claim 1, wherein A1 denotes methylene and A2 denotes methylene.

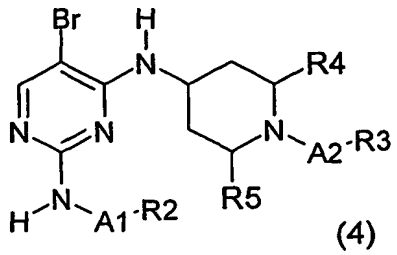
16. A pharmaceutical composition comprising a compound of the formula 1 as claimed in claim 1 and/or a pharmaceutically acceptable salt thereof together with pharmaceutically acceptable excipients and/or carrier.

17. A method of treating a patient afflicted with a disease or disorder, comprising the step of administering a therapeutically effective amount of a compound of the formula 1 as claimed in claim 1 and/or a pharmaceutically acceptable salt thereof to said patient afflicted with said disease or disorder, wherein the disease or disorder is selected from the group of acute and/or chronic airway disorders, inflammatory or allergen-induced airway disorder, bronchitis, obstructive bronchitis, spastic bronchitis, allergic bronchitis, allergic asthma, bronchial asthma, emphysema, chronic obstructive pulmonary disease (COPD), a disorder which is based on an excessive release of T-Cell derived cytokines, HIV-infection, septic shock, adult respiratory distress syndrome, graft-versus-host reactions, acute or chronic rejection of organ or tissue allo- or xenografts, generalized inflammations in the gastrointestinal area, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, allergic and/or chronic, faulty immunological reactions in the area of the upper airways and the adjacent regions, dermatose of the proliferative, inflammatory or allergic type, psoriasis (vulgaris), toxic and allergic contact eczema, atopic eczema, seborrheic eczema, lichen simplex, sunburn, pruritus in the anogenital area, alopecia areata, hypertrophic scars, discoid lupus erythematosus, follicular and wide-area pyodermias, endogenous and exogenous acne, acne rosacea, other proliferative, inflammatory, allergic skin disorders, a disorder in connection with disturbances of brain metabolism or alternatively disorders of the central nervous system (CNS), cerebral senility, senile dementia, multiinfarct dementia, depression, arteriosclerotic dementia, cancer and diabetes insipidus.

18. A method according to claim 17, in which a compound in claim 1 is used in combination with other therapeutic agents used in clinical practice for the treatment of the said disease or disorder.

19. A process for preparing a compound of formula 1 as claimed in claim 1 or a salt thereof, which comprises reacting a boronic acid derivative R1-$B(OH)_2$ wherein R1 has the meaning specified in

claim 1, with a pyrimidine derivate of formula (4)



(4)

in which A1, A2, R2, R3, R4 and R5 have a meaning specified in claim 1, and optionally converting an obtained compound into a corresponding salt or converting an obtained salt into a corresponding free compound.